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Ryan C. Ungaro, Michael D. Kappelman

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Reappraisal of COVID-19 Risk for Patients with Inflammatory Bowel Disease (IBD): Withdrawal of the British Society of Gastroenterology IBD Risk Grid

Commentary

Ryan C. Ungaro[1] and Michael D. Kappelman[2]

1. The Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, New York, USA
2. Division of Pediatric Gastroenterology, Department of Pediatrics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

Corresponding Author

Michael D. Kappelman, MD

Division of Pediatric Gastroenterology, Department of Pediatrics

University of North Carolina at Chapel Hill

Chapel Hill, North Carolina

michael_kappelman@med.unc.edu

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Early in the pandemic, there was significant concern about how COVID-19 may impact patients with inflammatory bowel disease (IBD). Would IBD, as a chronic immune-mediated condition, be a risk factor for more severe COVID-19? Would medications used to treat IBD, in particularly immunosuppressants, increase the likelihood of hospitalization or death due to COVID-19? However, at the start of the pandemic there was a paucity of data to guide decision making for patients with IBD. In this setting, many national and international societies issued statements on management of IBD to provide initial guidance to gastroenterologists and patients with IBD. The British Society of Gastroenterology (BSG) published an IBD risk grid for COVID-19 severity in April 2020 that proposed a framework for categorizing patients with IBD into those more likely to be vulnerable to COVID-19 primarily based on co-morbidities and disease characteristics.[1] Patients deemed at moderate risk were advised to practice stringent social distancing while those at high risk were recommended to practice "shielding," the strictest advice for isolating from others. The authors of the BSG IBD risk grid recently issued a statement withdrawing this guidance noting a number of factors including that the vast majority of IBD patients are not at increased risk of adverse COVID-19 outcomes, the reduced severity of disease with recent variants, and the effectiveness of COVID-19 vaccines.[2]

The decision to withdraw the BSG IBD risk grid is a reasonable and timely step as 1) our knowledge about the impact of COVID-19 on patients with IBD has greatly increased since the start of the pandemic, and 2) a number of "game changers" have dramatically altered the trajectory of the pandemic and natural history of COVID-19. These "game changers" include 1) development of highly effective and safe immunizations and booster strategies, 2) development of passive immunization or pre-exposure prevention with long-acting monoclonal antibodies, 3) a shift towards newer viral variants that appear to be produce infections that are less severe, and 4) emerging COVID-19 therapeutics that have been shown to reduce hospitalization and mortality when administered early in the course of infection.[3-5] Thus, we agree with BSG that advising

significant numbers of patients with IBD to “shield” or take strict social isolation precautions is overly stringent given the current state of the pandemic and our understanding of COVID-19 in IBD.

The most significant development in curbing the pandemic has been the introduction of safe and effective COVID-19 vaccines. Fortunately, the vast majority of patients with IBD respond well to immunization. A meta-analysis of over 40 studies demonstrated high rates of seroconversion in patients with IBD following COVID-19 vaccination.[6] Real world studies have also demonstrated that the real-world effectiveness of COVID-19 vaccines against infection is similar in IBD and matched controls.[7] Although certain factors such as TNF antagonist treatment, combination therapy and corticosteroids have been associated with lower humoral response, these can be mitigated with additional doses of COVID-19 vaccine.[8-10]

More recently, a long-acting monoclonal antibody [Tixagevimab–Cilgavimab (Evusheld)] has been FDA approved for pre-exposure prevention of COVID-19 and has been shown to benefit individuals at risk of poor response to immunization, such as patients with moderate to severe immune suppression.[3] Specifically, a single IM dose reduced the risk of developing symptomatic COVID-19 by 77%. Although pre-exposure prevention is likely not necessary for the majority of patients with IBD, it’s use should be considered in certain patients at higher risk for non-response to primary vaccination such as those treated with corticosteroids and combination immunotherapy at the time of vaccination. As society continues to return to a “new-normal” the use of passive immunization strategies in addition to active immunization can be an alternative to “shielding” in the most vulnerable patients.

Finally, COVID-19 therapies such as paxlovid, molnupirivir, remdesivir, and emerging monoclonals that improve recovery time and decrease hospitalization and death are now more

widely available and can be offered to patients with IBD.[5] We believe that these newer therapeutics that attenuate the course of COVID-19 further call in to question the need for strict physical distancing and can further provide patients reassurance that they can safely but cautiously return to normal.

Reassuringly, IBD patients do not appear to be at increased risk of contracting COVID-19 and as a whole are not at increased risk of adverse COVID-19 events.[11-14] However, we and others have identified a number of risk factors for severe COVID-19 in patients with IBD. As in the general population, risk factors for patients with IBD include older age, multiple co-morbidities in addition to IBD, and non-White race.[15,16] The highest risk non-IBD co-morbidities in IBD patients appear to be chronic kidney disease and chronic obstructive pulmonary disease.[17] IBD-related risk factors for severe COVID-19 include moderately to severely active disease (by physician global assessment), corticosteroid use, and combination of tumor necrosis factor (TNF) antagonists with thiopurines.[18,19] It should be noted that risk of combination therapy appears to be specific to thiopurines and not methotrexate and that there are conflicting data on this association.[19,20] Although we agree with the BSG IBD risk grid authors that the use of the broad IBD risk grid is no longer warranted and may cause undue anxiety, we instead advocate that a more individualized approach that takes these patient and treatment-related factors into account may still be valuable. Patients with one or more of these risk factors may consider consistent use of high-quality masks in public spaces or avoiding large events in areas of high COVID-19 incidence. Additionally, these risk factors can be used in conversations with patients who are vaccine hesitant and in making decisions about pre-exposure prevention and use of COVID-19 therapeutics.

Implementing risk grids is a dynamic process based on evolving data and needs to be revisited depending on the direction of the pandemic. We applaud the BSG IBD risk grid authors for updating their guidance regarding need for shielding and social distancing as we enter a new

phase of the pandemic. Increased knowledge of risks related to IBD and COVID-19 has largely been reassuring. The introduction of effective vaccines, strategies for pre-exposure prevention, and safe and effective therapies have resulted in the pandemic now impacting most patients with IBD in a similar fashion as the general population.

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